97. (new) An isolated nucleic acid sequence comprising a nucleotide sequence of SEQ ID NO:12 or SEQ ID NO:13.

Pcancid

98. (new) An isolated nucleic acid sequence that encodes a polypeptide comprising a amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4.

REMARKS

With this amendment, claims 32-35, 37-40, 46, 47, and 94-98 are pending and under examination. Claims 1-31, 41-45, and 48-93 are currently withdrawn from consideration as non-elected inventions. Claim 36 has also been canceled without prejudice to subsequent revival. New claims 94-98 have been added. The amended claims are provided in Appendix A, Version with Markings to Show Change. All pending claims are provided in Appendix B. Applicants address the Examiner's rejections in the order presented in the November 7, 2000 Office Action.

Status of the claims

Claim 37 has been amended to recite stringent hybridization conditions. This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 21, lines 27-29.

Claim 38 has been amended to recite moderately stringent hybridization conditions. This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 22, line s1-2.

New claims 94-98 have been added. These claims add no new matter. Support for these claims can be found, e.g., in the claims as originally filed, and in the specification on page 8, line 16-17, page 21, lines 27-29, and page 22, line s1-2.

Rejection under 35 U.S.C. § 101 and 35 U.S.C. § 112: utility

Claims 32-40, 46, and 47 were rejected as allegedly supported neither by a specific and substantial utility, nor by a well-established utility. Applicants respectfully traverse the rejection.

As described in the present specification, full length cDNAs that encode a taste cell-specific polypeptide were cloned, and mRNA expression patterns were determined for the clones using *in situ* assays of tongue tissue (*see, e.g.*, Example 1, page 54-55). The claimed nucleic acids, full length cDNAs encoding a protein, are rare transcripts that are preferentially expressed in a subset of taste receptor cells, specifically the Gustducin-expressing taste receptor cells of the circumvallate and foliate papillae of the tongue (*see, e.g.*, specification, page 8, lines 20-24).

The nucleic acids of the present invention are therefore useful, e.g., as taste cell specific markers because the nucleic acids and the proteins that they encode are specifically expressed in specialized taste cells of the tongue (*see, e.g.*, specification, page 6, lines 15-19). For example, such taste cell specific molecules serve as invaluable tools in the generation of taste topographic maps that elucidate the relationship between taste cells of the tongue and taste sensory neurons leading to taste centers in the brain (*see, e.g.*, specification, page 6, lines 19-22). Such maps are useful in pharmacological and food industries for customizing taste. This use is not merely a starting point for "further experimentation." The nucleic acids of the invention therefore have specific, substantial, and credible utility. Applicants therefore respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph: enablement

A. Introduction

Claims 32-40, 46, and 47 were rejected as allegedly enabled in scope only for polynucleotides encoding a polypeptide of SEQ ID NO:3 or SEQ ID NO:4, but not for polynucleotides encoding polypeptides having about 70% identity to SEQ ID NO:3 or SEQ ID NO:4. See Office Action, page 4. Applicants respectfully traverse the rejection.

As identified in the Patent Office and the Federal Circuit, whether undue experimentation is required by one skilled in the art to practice to invention is determined by

considering factors such as the amount of guidance presented in the application, the state of the prior art, and the presence of working examples. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, a "considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should precede." *Wands*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982).

The claims as amended now specify hybridization conditions, as well as conserved reference sequences to which the claimed nucleic acids must hybridize or have a certain percent identity. Hybridization methods for the identification of nucleic acids are also are well known to those of skill in molecular biology, as well as sequence algorithms for determining percent identity to a given reference sequence. These elements therefore provide adequate guidance for routine identification of the nucleic acids of the invention. Finally, Applicants clearly meet the PTO guidelines for enablement, which set forth the standard for the scope of enablement when a large number of possible embodiments exists. Thus, undue experimentation is not required to practice the claimed invention.

B. The claimed reference sequences provide a meaningful structural feature that allows one of skill to identify the claimed sequences without undue experimentation

The rejection alleges that the specification provides enablement only for identifying nucleic acids encoding a taste cell specific polypeptide having an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4. However, the claims recite structural and functional characteristics of the taste cell specific polypeptides encoded by the nucleic acids of the invention and assays for identification of the claimed nucleic acids having the recited structural features. The assays and examples of the specification, together with standard methodology known to those of skill in the art, therefore provide adequate guidance for identifying nucleic acids encoding the nucleic acids of the invention, without undue experimentation.

The assertion of undue experimentation appears to be based on an assumption that enablement requires the description of each and every nucleic acid that could be covered in the

invention. As noted below, such a requirement is not consistent with the patent laws. Indeed, it is well settled in the biotechnology art that routine screening of even large numbers of samples is not undue experimentation when a probability of success exists. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Using the conditions set forth in the claims and specification and routine methodology, any competent laboratory technician in a molecular biology laboratory could isolate and prepare appropriate constructs, transform cells, and identify those nucleic acids that encode a G protein gamma subunit protein of the invention. As set forth in MPEP § 2164.08, a rejection for undue breadth is inappropriate where "one of skill could readily determine any one of the claimed embodiments." In the present case, one of skill, given the conserved amino acid and nucleotide sequences, sequence algorithms, and the specified hybridization conditions, could easily screen for other nucleic acid and protein molecules that fall within the scope of the claims.

The present invention describes a family of nucleic acids encoding taste specific polypeptides which structurally either: (1) hybridize to reference nucleic acids; or (2) have greater than about 70% identify to reference nucleic acids. Furthermore, the claimed nucleic acids are preferentially expressed in a subset of taste receptors cells, namely, the circumvallate and foliate papillae.

At the time of the present invention, identification of nucleic acids having the structural characteristics described above was well within the means of one of skill of the art, without undue experimentation. The present specification provides working examples and discloses standard techniques known to those of skill in the art, for the identification of taste cell specific polypeptides having at least about 70% identity to an amino acid sequence SEQ ID NO:3 or SEQ ID NO:4. For example, one of skill in the art could use standard manual or computer sequence alignment to determine whether potential sequences have the specified identity (*see, e.g.*, specification, pages 18-20). In addition, one of skill in the art could use standard hybridization and PCR assays to identify nucleic acids encoding the polypeptides of the invention (*see, e.g.*, specification, pages 25-27).

The assays described in the specification, coupled with methodology well known to those of skill in the art, therefore demonstrate that screening for nucleic acids encoding a taste cell specific polypeptide having the structural and functional characteristics described above is

routine. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants therefore respectfully request that the rejection be withdrawn.

C. One of skill in the art could readily determine any one of the claimed nucleic acids

Finally, regarding the issue of enablement for nucleic acids, where a large number of possible embodiments exist, the PTO has provided express guidelines for examination. As set forth in the MPEP § 2168.08, a rejection of such claims such as those in the present application for undue breadth is inappropriate where one of skill could readily determine any one of the claimed embodiments.

This standard is further explained in the "Training Materials for Examining Patent Applications with respect to 35 U.S.C. § 112, first paragraph – Enablement Chemical/Biotechnological Applications," section III.A.2.b.i(c). In the guidelines, the PTO specifically answers the question regarding scope of a nucleic acid composition claim (e.g., in the present case, a nucleic acid encoding a taste cell specific polypeptide) left open by the Federal Circuit in *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995). The claims at issue in *Deuel* were directed to any DNA encoding a specific amino acid sequence. Thus, a great number of nucleic acids were within the scope of the claims. In fact, the number was so great that a listing of all possible DNAs encoding the protein was a practical impossibility.

In the guidelines, the PTO addressed this issue, explaining that "even though a listing of all possible DNAs which encode a given protein is a practical impossibility due to the enormous number of such nucleic acids, any particular sequence can be written by one of skill given the disclosure and the sequence can be ordered from a company which synthesizes DNA." In this manner, one of skill in the art can readily determine any one of the embodiments. The PTO concluded that scope rejections such as the one hypothesized in *Deuel* should not be advanced.

In the present application, one of skill in the art has only to identify nucleic acids that either (1) hybridize under specified conditions to conserved reference nucleotide sequences of SEQ ID NO:12 or SEQ ID NO:13; (2) are amplified by the primers that hybridize under specified conditions to the conserved reference sequence, using techniques described in the

specification or known to those of skill in the art, or (3) use well known sequence algorithms to identify nucleic acids that have at least 70% identity to a conserved reference sequence of SEQ ID NO:3 or SEQ ID NO:4. Although many such nucleic acids are possible, one of skill can readily determine, one by one, any particular inward rectifier encoding nucleic acid, without undue experimentation. For example, nucleic acid screening, hybridization, and PCR techniques are described in the specification and the art, as described above. Furthermore, one of skill can use the assays described above to test the functionality of the protein encoded by the nucleic acid of interest and easily determine if it falls within the scope of the claims. Thus, in the present application the skilled artisan can readily, with only routine experimentation, make and test any particular inward rectifier encoding nucleic acid.

The specification, combined with the state of the prior art, thus provides a number of different assays demonstrating that any experimentation required to identify nucleic acids encoding taste cell specific polypeptide is not undue. *In re Wands*, 8 USPQ 1400 (Fed. Cir. 1988). Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph: written description

Claim 36 was rejected as allegedly lacking written description. Claim 36 has been canceled, so the rejection is moot. Applicants request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Annette S. Parent

Annette S. Parent
Reg. No. 42,058

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
SF 1204854 v1

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGE

39. (once amended) An isolated nucleic acid encoding a sensory cell specific polypeptide that specifically hybridizes under highly stringent conditions to a nucleic acid having the sequence of SEQ ID NO:12 or SEQ ID NO:13, wherein the hybridization reaction is incubated at 42°C in a solution comprising 50% formamide, 5x SSC, and 1% SDS and washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS.

40. (once amended) An isolated nucleic acid encoding a sensory cell specific polypeptide, the polypeptide comprising greater than about 70% amino acid sequence identity to an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4, wherein said nucleic acid selectively hybridizes under moderately stringent hybridization conditions to a nucleotide sequence of SEQ ID NO:12 or SEQ ID NO:13, wherein the hybridization reaction is incubated at 37°C in a solution comprising 40% formamide, 1 M NaCl, and 1% SDS and washed at 45°C in a solution comprising 1x SSC.

94. (new) An isolated nucleic acid encoding a sensory cell specific polypeptide comprising an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4 or an antigenic fragment thereof.

95. (new) An isolated nucleic acid encoding a sensory cell specific polypeptide, wherein the polypeptide has a predicted molecular weight of approximately 85 KDa, and wherein the nucleic acid specifically hybridizes under stringent hybridization conditions to a nucleic acid having the sequence of SEQ ID NO:12 or SEQ ID NO:13, wherein the hybridization reaction is incubated at 42°C in a solution comprising 50% formamide, 5x SSC, and 1% SDS and washed at 65°C in a solution comprising 0.2x SSC and 0.1% SDS.

96. (new) An isolated nucleic acid encoding a sensory cell specific G polypeptide comprising greater than about 70% amino acid identity to a polypeptide comprising

an amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4, which polypeptide has a predicted molecular weight of approximately 85 KDa.

97. (new) An isolated nucleic acid sequence comprising a nucleotide sequence of SEQ ID NO:12 or SEQ ID NO:13.

98. (new) An isolated nucleic acid sequence that encodes a polypeptide comprising a amino acid sequence of SEQ ID NO:3 or SEQ ID NO:4.